

**UNITED STATES DISTRICT COURT
DISTRICT OF DELAWARE**

CAREDX, INC.)	
)	
Plaintiff,)	
)	C.A. No. 19-662 (CFC)
v.)	
)	JURY TRIAL DEMANDED
NATERA, INC.,)	
)	
Defendant.)	

**CAREDX’S OPENING BRIEF IN SUPPORT OF ITS MOTION FOR
JUDGMENT AS A MATTER OF LAW UNDER FRCP 50**

Dated: April 4, 2022

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TABLE OF CONTENTS

	<u>Page</u>
I. INTRODUCTION	1
II. NATURE AND STAGE OF PROCEEDINGS.....	2
III. LEGAL STANDARD	3
IV. ARGUMENT.....	4
A. Natera Advertises That Prospera Can Detect TCMR And AlloSure Cannot.....	4
B. CareDx Proved The TCMR Advertisement Violates The Lanham Act	5
1. CareDx Proved The TCMR Advertisement Is Literally False	5
a. Natera’s Own Executives And Specialists Agreed That The TCMR Advertisement Is Unsupported And Thus It Is Literally False.....	6
b. Unrebutted Testimony Also Proved The Unreliability Of The Sigdel Study.....	10
c. The Cited Studies Do Not Support The Claim Made	11
d. Natera’s Trial Testimony Is Not Substantial Evidence For Its TCMR Advertisement.....	11
2. CareDx Proved That The TCMR Advertisement Is Material And Likely To Injure CareDx.	13
V. CONCLUSION.....	16

TABLE OF AUTHORITIES

Page(s)

Cases

<i>Bracco Diagnostics, Inc. v. Amersham Health, Inc.</i> , 627 F. Supp. 2d 384 (D.N.J. 2009)	14
<i>Castrol Inc. v. Pennzoil Co.</i> , 987 F.2d 939 (3d Cir. 1993)	13
<i>Castrol, Inc. v. Pennzoil Quaker State Co.</i> , 169 F. Supp. 2d 332 (D.N.J. 2001)	5
<i>Gardner-Lozada v. SEPTA</i> , 643 F. App'x 196 (3d Cir. 2016)	3
<i>Johnson v. Campbell</i> , 332 F. 3d 199 (3d Cir. 2003)	3
<i>Pernod Ricard USA, LLC v. Bacardi U.S.A., Inc.</i> , 653 F.3d 241 (3d Cir. 2011)	5
<i>Telebrands Corp. v. E. Mishan & Sons</i> , No. 97–1414, 1997 WL 232595 (S.D.N.Y. May 7, 1997)	13

Statutes

Delaware Deceptive Trade Practices Act, 6 Del. C. § 2532(a)	2, 3
Lanham Act, 15 U.S.C. § 1125(a)	<i>passim</i>

Other Authorities

FRCP 50(a)	3
FRCP 50(b)	2

I. INTRODUCTION

CareDx, Inc. (“CareDx”) revolutionized the standard of care for kidney transplant patients with its AlloSure blood test, which allows for non-invasive and accurate detection of organ rejection. CareDx invested tens of millions to develop AlloSure and educate the transplant community about this radical new approach. In 2019, after CareDx had established this game-changing medical diagnostic, Natera, Inc. (“Natera”) launched a copy-cat test, Prospera. Although Natera had been working with cell-free DNA for many years to make blood tests, it had not entered the organ rejection space until CareDx paved the way at great expense.

Rather than promoting Prospera to transplant clinicians who did not yet use cell-free DNA, and grounding its advertising in sound science, Natera chose a different strategy. Natera created a marketing campaign with a central plank – the conversion of AlloSure customers to Prospera. To accomplish this AlloSure customer-conversion strategy, Natera promoted a core marketing message: the false assertion that Prospera performed even *better* than AlloSure. Natera developed marketing materials predicated on head-to-head comparisons and claims of superiority without having reliable scientific and statistical support for these comparisons. Natera then systematically trained its sales force to sell to doctors by characterizing its supposed superior performance featured in its advertising as based on an “apples to apples” statistical comparison. Mar. 9, 2022 Rough Tr. 91:6-10.

These false claims of superiority formed the basis for CareDx's false advertising claims against Natera. And, after a five-day jury trial, the jury correctly found that CareDx proved that nine out of ten advertising claims made by Natera are literally false with the lone exception being Natera's claims related to t-cell mediated rejection ("TCMR").

Although overturning a jury verdict pursuant to a FRCP 50(b) motion is extraordinary, here the record is so overwhelming as to Natera's TCMR advertising claims that a narrow reversal is warranted on that one verdict question. Like all of Natera's other advertising claims, Natera's TCMR advertising is false.

Specifically, the uncontradicted evidence, including admissions of top Natera employees and Natera's own expert, demonstrates that Natera's TCMR comparison, just like its other comparisons, is false advertising. Despite these admissions, Natera still advertises that Prospera can detect TCMR and AlloSure cannot. Accordingly, the extraordinary relief of JMOL is appropriate here on this one limited ground to help stop this false advertising.

II. NATURE AND STAGE OF PROCEEDINGS

On April 10, 2019, CareDx initiated this action against Natera, alleging (1) false advertising under the Lanham Act (15 U.S.C. § 1125(a)), (2) Unfair Competition under Delaware Law, and (3) violations of the Delaware Deceptive Trade Practices Act (the "DTPA") (6 Del. C. § 2532(a)). D.I. 1. After this court

granted-in-part and denied-in-part Natera's motion to dismiss (*see* D.I. 40), CareDx filed its First Amended Complaint on February 7, 2020. D.I. 45.

In Natera's Amended Answer and Counterclaims, its operative pleading for trial, Natera denied liability and alleged counterclaims that CareDx (1) engaged in false advertising under the Lanham Act (15 U.S.C. § 1125(a)), (2) violated the DTPA (6 Del. C. § 2532(a)), and (3) engaged in Unfair Competition under Delaware state law. D.I. 159.

A five-day jury trial began on March 7, 2022. On March 14, 2022, the jury returned its verdict. D.I. 329. The jury found for CareDx on all of its claims save one: that Prospera can detect TCMR and AlloSure cannot (the "TCMR Advertisement"). D.I. 329-12 (CareDx Question No. 9).

III. LEGAL STANDARD

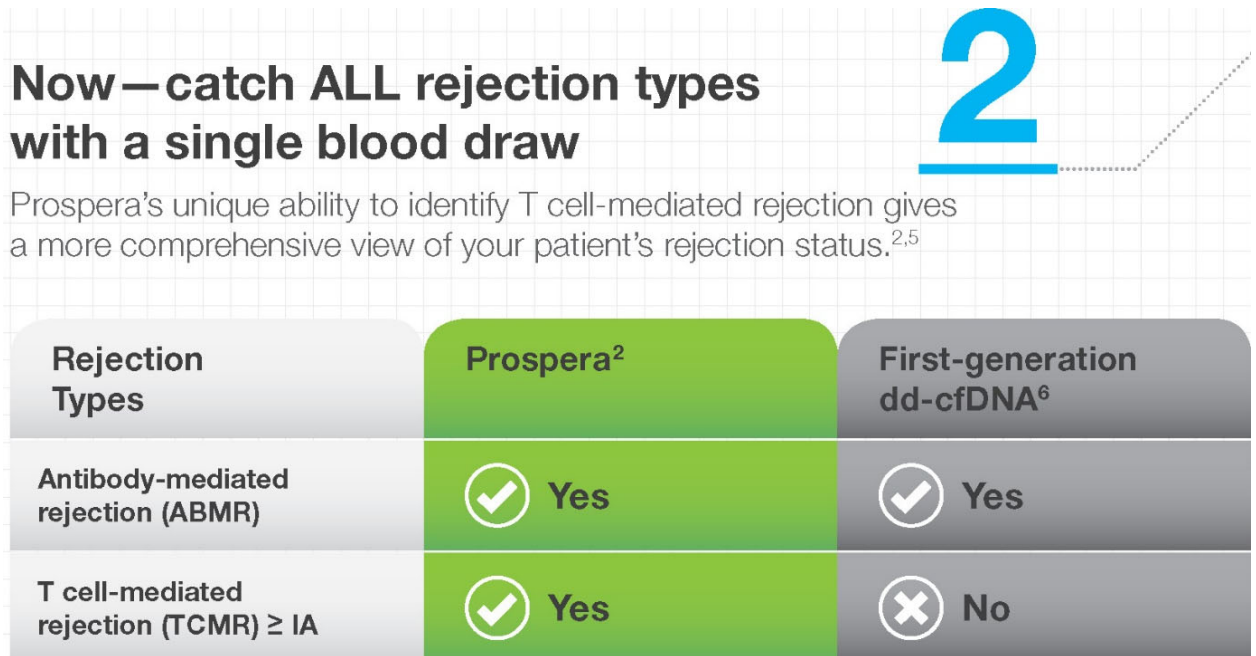
A court may grant judgment as a matter of law only when "a reasonable jury would not have a legally sufficient evidentiary basis to find for the party on that issue." *Gardner-Lozada v. SEPTA*, 643 F. App'x 196, 198 (3d Cir. 2016) (quoting FRCP 50(a)). The Court must consider "whether, 'viewing the evidence in the light most favorable to the verdict, a reasonable jury could have found for the prevailing party.'" *Gardner-Lozada*, 643 App'x at 198 (quoting *Johnson v. Campbell*, 332 F. 3d 199, 204 (3d Cir. 2003)).

IV. ARGUMENT

The Jury found that Natera is not liable for false advertising for its TCMR Advertisement. But the overwhelming evidence demonstrates that the TCMR Advertisement is false advertising under the Lanham Act. The jury's verdict with respect to the TCMR Advertisement therefore fails as a matter of law.

A. Natera Advertises That Prospera Can Detect TCMR And AlloSure Cannot

As this graphic from the “money spread” in Natera's Physicians' Brochure shows, Natera categorically advertises that Prospera can detect TCMR and that AlloSure cannot:



Now—catch ALL rejection types with a single blood draw

Prospera's unique ability to identify T cell-mediated rejection gives a more comprehensive view of your patient's rejection status.^{2,5}

Rejection Types	Prospera ²	First-generation dd-cfDNA ⁶
Antibody-mediated rejection (ABMR)	✓ Yes	✓ Yes
T cell-mediated rejection (TCMR) ≥ IA	✓ Yes	✗ No

JTX7-3. Natera based this claim on its own Sigdel study of Prospera and the Bloom and Huang papers which assessed AlloSure. JTX1; JTX2; DTX5.

B. CareDx Proved The TCMR Advertisement Violates The Lanham Act

CareDx has established beyond cavil that: 1) the TCMR Advertisement is literally false (and therefore no proof of actual deception is required); and 2) the false TCMR Advertisement is material, and there is a likelihood of a resultant injury to CareDx. *See Pernod Ricard USA, LLC v. Bacardi U.S.A., Inc.*, 653 F.3d 241, 248 (3d Cir. 2011) (discussing elements of a Lanham Act claim).¹

1. CareDx Proved The TCMR Advertisement Is Literally False

CareDx showed that the TCMR Advertisement, which claims that Prospera detects TCMR and AlloSure does not, is false because: (1) Natera admitted that the studies on which the advertising claim was based were not sufficiently reliable to permit this conclusion; (2) CareDx introduced un rebutted evidence that further demonstrated the unreliability of Natera's study; (3) even if the studies were reliable, they do not support the claim made; and (4) trial testimony from Dr. Christians and Dr. Gauthier does not disturb this conclusion. Final Jury Instruction 3.3; *see also Castrol, Inc. v. Pennzoil Quaker State Co.*, 169 F. Supp. 2d 332, 336 (D.N.J. 2001).

¹ Natera does not dispute that the statements in the TCMR Advertisement were made in interstate commerce or that CareDx is entitled to a presumption of actual deception if CareDx proves the TCMR Advertisement is literally false. Mar. 14, 2022 Tr. at 5:21-8:17.

a. Natera's Own Executives And Specialists Agreed That The TCMR Advertisement Is Unsupported And Thus It Is Literally False

Natera's TCMR Advertisement is inconsistent with the supposedly supporting studies and thus lacks reliable support. Final Jury Instruction 3.3; Mar. 14, 2022 Tr. 51:8-13 ("And something is literally false -- this is important because this is a bit of a twist to it. If the challenge advertisement implicitly or explicitly refers to studies or data establishing a particular claim where -- you know, whatever the advertising claim is is literally false if the studies are not sufficiently reliable. Let me go back. Sufficiently reliable to permit a conclusion or even though they are reliable, they do not establish the claim asserted by the defendant.").

Natera's own Dr. Allison Ryan admitted as much. Dr. Ryan earned a PhD. and was Vice President of R&D Data Science leading Natera's data science group of 20-30 data science specialists. Mar. 8, 2022 Rough Tr. 95:13-16, 96:2-16. Dr. Ryan was responsible for reviewing proposed Prospera marketing materials to evaluate Natera's advertising claims for "scientific accuracy." *Id.* at 96:9-16.

In discussing the very Physicians' Brochure in which Natera's TCMR Advertisement is published and other Prospera marketing materials, Dr. Ryan was adamant that it was improper for Natera to advertise that Prospera *can* detect TCMR and CareDx *cannot* detect TCMR because that claim was totally unsupported—much less reliably supported as required by law. In November 2018, Dr. Ryan

informed Jonathan Sternberg (Natera’s Senior Product Manager for Prospera) that, Natera “should NOT form a market strategy based on the idea that we detect TCMR and they [CareDx] don’t.” PTX70-3 (capitalization-in-original). Dr. Ryan stated that there was no support for Natera’s advertising claim: “We do ***not*** have statistical evidence that we have any advantage here.” PTX70-3.²

Other Natera leaders concurred with Dr. Ryan’s assessment. In response to Dr. Ryan’s explicit warning, Mr. Sternberg met with the leadership of Natera’s Organ Transplant business, including Adam Prewett (the Prospera Product Manager) and Dr. Solomon Moshkevich (the overall head of the Natera Organ Transplant business), to discuss Dr. Ryan’s conclusion that the proposed advertising claim was unsupported. PTX70-1.

In view of the lack of scientific support, they “all agreed that the correct, scientifically and otherwise, thing to do [in the “physicians’ brochure and other marketing materials”] is to simply describe the data as we’ve seen it, speaking about the results in a study-specific matter.” *Id.* In response, Dr. Ryan agreed with this approach. *Id.* At this time, of the two AlloSure focused papers ultimately cited in the TCMR Advertisement, only the Bloom paper had been published. JTX2.

² Emphasis supplied throughout unless otherwise specified.

In January 2019, the Huang paper was published. DTX5. In March 2019, even after publication of the Huang paper, Dr. Ryan reiterated that it was simply improper to assert that AlloSure “can’t” detect TCMR: “[t]he conclusion was that it is very reasonable to point out that we had better TCMR detection in the small data sets in Bloom and Sarwal, but *we should not* make any stronger claims along the lines of ‘*our technology can detect it and theirs can’t*.’” PTX71-2. Adam Prewett, the Prospera Product Manager, responded that “All we can talk about is *our* data and it should be highlighted.” PTX71-1.

Dr. Ryan was not alone among Natera’s data experts in concluding that Natera’s TCMR Advertisement was unsupported. Dr. Felipe Acosta is a Lead Data Scientist at Natera, and was the primary person involved in the Prospera data analysis. Mar. 8, 2022 Rough Tr. 106:13-19. Dr. Acosta flatly admitted that Natera could not claim any statistical difference in detecting TCMR between Prospera and AlloSure because of the tiny (10-16 patients) sample size:

- Q.** Okay. You don’t disagree with Dr. Ryan’s statements here regarding TCMR, correct?
- A.** What do you mean? Disagree with what statement?
- Q.** Her statement that Natera doesn’t have an advantage in detecting TCMR relative to CareDx?
- A.** I mean, this is based on *10 to 16 samples*, so I would say that this specific study, yeah, it does not show that we can claim statistical difference between the two.

Id. at 112:12-19.

Dr. Acosta explained that the 10-16 patient sample size is insufficient to support a claim of performance differences in detecting TCMR, much less that AlloSure just cannot detect TCMR:

Q. I'm saying based on what you know about what the sample sizes were, would you be comfortable making comparison between the sensitivity of the Natera test and the sensitivity of the CareDx test?

A. ***So based on what I know about the sample sizes, that's not enough information for me to claim differences or not.***

Id. at 116:18-24.

Internally, Natera's leadership never deviated from Dr. Ryan's directive that the TCMR Advertisement was unsupported and that the Physicians' Brochure should not state that Prospera can detect TCMR and AlloSure cannot. This makes sense because Dr. Ryan was the executive ultimately responsible for reviewing the Prospera marketing materials for "scientific accuracy." Mar. 8, 2022 Rough Tr. 96:9-16.

Dr. Ryan confirmed that she could not recall "any change in opinion" after her November 2018 email:

Q. At any point in time, did your recommendation that Natera should not form a market strategy based on the idea that Natera detects TCMR and CareDx does not change?

A. I don't remember communicating any change in opinion with respect to what's stated here afterward.

Mar. 8, 2022 Rough Tr. 103:12-16; *see also id.* at 105:3-5.³

The undisputed evidence proved there was consensus among Natera executives including Natera's Vice President of R&D Data Science, its Data Specialist for Prospera, its Prospera Senior Product Manager, its Prospera Product Manager, and the head of the entire Natera Organ Transplant business that it was not "correct" to advertise in the Physicians' Brochure that Prospera could detect TCMR and AlloSure could not.

b. Unrebutted Testimony Also Proved The Unreliability Of The Sigdel Study

At trial, CareDx introduced unrebutted testimony from Dr. Robert Woodward, CareDx's Senior Vice President of Research and Development, that further showed that Natera's TCMR comparison is faulty and false because of differences between study designs.

Dr. Woodward testified that: (1) Natera's claim as to its own TCMR capability did not use the standard definition for TCMR 1A and instead "only use[d] the most severe of those rejections." Mar. 14, 2022 Tr. 38:25-39:7, 42:3-9; and (2) in contrast, CareDx did not "preselect any samples," in its DART study and "[t]here was a

³ Dr. Phillipe Gauthier, Natera's Medical Director, likewise testified that he was not aware of anyone that redid Dr. Ryan's analysis and came to a different conclusion. Mar. 9, 2022 Rough Tr. at 65:21-66:8.

complete range of severity of TCMR.” *Id.* at 33:6-12. Natera never attempted to rebut this fundamental flaw in the reliability of the Sigdel study to support Natera’s TCMR Advertisement.

c. The Cited Studies Do Not Support The Claim Made

Even if the Sigdel study and Bloom and Huang papers somehow provided a reliable basis for this type of claim, these studies do not support Natera’s categorical TCMR claim that Prospera can detect TCMR and AlloSure cannot.

This is because the Bloom and Huang papers show that AlloSure can indeed detect rejection in TCMR samples. In Bloom, AlloSure detected rejection in three of eleven TCMR samples utilizing a 1% threshold. JTX2-8, Figure 4. Similarly, in Huang, AlloSure detected rejection in three of ten TCMR samples utilizing a 1% threshold. DTX5-3.

d. Natera’s Trial Testimony Is Not Substantial Evidence For Its TCMR Advertisement

At trial, Natera’s expert Dr. Christians and Natera employee Dr. Gauthier testified in support of Natera’s TCMR claim. Their testimony does not provide substantial evidence supporting the claim.

First, Dr. Acosta, who was directly responsible for the Prospera statistical analysis, was definitive that 10-16 samples was simply too small to infer a “statistical difference” in TCMR performance. Mar. 8, 2022 Rough Tr. 112:12-19.

Second, Dr. Christians admitted that he could not say there was a statistically significant difference between AlloSure and Prospera in TCMR detection because “nobody tested . . . significant difference between the Natera and CareDx paper.” Mar. 10, 2020 Tr. 95:22-96:3. Indeed, Dr. Christians admitted that there was no basis to claim better performance much less significantly better performance between the two tests:

Q. And do you agree with Elizabeth Mihok's conclusion as Natera's senior program manager that the statistical does not -- the statistical analysis does not support claims of significantly better performance by Prospera versus AlloSure?

A. I completely agree with her because it was never statistically compared. So I would take the ‘significantly’ out of there too.

Id. at 94:1-9.

Third, while Dr. Gauthier incredibly testified that he had found a statistically significant difference where Natera's expert statisticians and its testifying expert had found none, Dr. Gauthier's testimony does not support Natera's TCMR Advertisement. Mar. 9, 2020 Rough Tr. 39:24-40:10. This definitively-controverted and unexplained lay opinion testimony is conclusory and thus not substantial evidence.

Moreover, it would, at most, support a claim of superiority, not that Prospera could detect TCMR and AlloSure could not. This is because Dr. Gauthier

acknowledged under examination from counsel for Natera that AlloSure can detect TCMR:

Q: Now, you referred to some data with ten out of ten compared to three out of eleven. Do you remember that?

A. Yes.

Q. Can you tell the jury what you were talking about?

A. Sure. So in our study, we had ten cases of T-cell rejection, and our test was positive for all ten; so we detected all of them. In their study [Bloom] they had 11 cases of T-cell rejection and they only detected three.

Id. at 47:2-16.

At bottom, there is simply overwhelming evidence from the very top experts and business leaders at Natera itself, not to mention common sense, that Natera lacked reliable scientific support for its TCMR advertising claim. Even Dr. Christians admitted that there is no statistical support for a claim that Prospera is superior to AlloSure in detecting TCMR, as quoted above. That should end the matter.

The only reasonable conclusion for the jury based on the trial record is that the TCMR Advertisement is literally false.

2. CareDx Proved That The TCMR Advertisement Is Material And Likely To Injure CareDx.

CareDx is entitled to a presumption of materiality because it proved Natera's statements are literally false. Final Jury Instructions 3.4; *see also Castrol Inc. v.*

Pennzoil Co., 987 F.2d 939, 950-51 (3d Cir. 1993) (finding that a plaintiff must not prove an advertisement is material, in that it is likely to influence purchasing decisions, where an advertisement is literally false); *Bracco Diagnostics, Inc. v. Amersham Health, Inc.*, 627 F. Supp. 2d 384, 478 (D.N.J. 2009) (“Once it is determined that a statement is false, it is presumed to be material.”) (quoting *Telebrands Corp. v. E. Mishan & Sons*, No. 97–1414, 1997 WL 232595, at *22 (S.D.N.Y. May 7, 1997)). Natera has not rebutted the presumption that the TCMR Advertisement is material and, in fact, Natera touted at trial the importance of TCMR detection to its Prospera marketing.

The testimony of Natera’s own expert, Dr. Christians, proves that the TCMR Advertisement “is likely to influence purchasing decisions”:

Q. You believe that being able to publicize that you have an advantage in TCMR detection could have a big – make a big commercial difference, correct?

A. Yes.

Q. And you are the target audience for Natera and CareDx’s product, correct?

A. Yes.

Mar. 10, 2022 Tr. 96:9-15.

The uncontradicted evidence also shows that there is a likelihood of injury to CareDx as a result of the false TCMR Advertisement. First, CareDx proved, and Natera agrees, that TCMR data is important to physicians. Again, Dr. Christians

testified that he is the “target audience” and that TCMR detection could “make a big commercial difference.” *Id.* Moreover, Adam Prewett, Natera’s Prospera Product Manager, wrote in a March 10, 2019 email that “whenever we mentioned we detected TCMR in our study clinicians jumped on it, I literally saw ears perk up.” PTX71-1. Mr. Prewett also testified that Natera knows its “audience, transplant surgeons and nephrologists, are very data-driven.” Mar. 9, 2022 Rough Tr. 93:3-10.

Second, CareDx proved that the TCMR Advertisement was a key marketing piece used to get transplant centers using AlloSure to switch to Prospera. One of the undisputed goals of Natera’s marketing plan is to “CONVERT ALLOSURE USERS TO PROSPERA USERS.” PTX141-3. The TCMR Advertisement is included in Natera’s Physician’s Brochure. *See* JTX7-3. Natera’s Marketing Director, Shephalie Lahri, testified that the Physician’s Brochure is Natera’s “primary marketing piece” and referred to internally at Natera as the “money spread.” *See* Mar. 8, 2022 Rough Tr. 297:1-2, 298:21-23. And Natera’s expert, John Plumpe, confirmed that Natera referred to the Physician’s Brochure as the money spread because “that’s how they got money.” Mar. 10, 2022 Tr. 278:2-8.

Thus, the undisputed evidence demonstrates that the TCMR Advertisement made false statements about a key performance metric and is therefore likely to injure CareDx.

V. CONCLUSION

For the foregoing reasons, CareDx asks the Court to enter JMOL that the TCMR Advertisement (CareDx Question No. 9, D.I. 329-12) violates the Lanham Act.

Dated: April 4, 2022

Respectfully submitted,

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CERTIFICATION OF COMPLIANCE

The foregoing document complies with the type-volume limitation of this Court's March 2, 2020 form Scheduling Order for All Cases. The text of this brief, including footnotes, was prepared in Times New Roman, 14 point. According to the word processing system used to prepare it, the brief contains 3,171 words, excluding the case caption, signature block, table of contents and table of authorities.

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